

Acute Heart Failure Syndromes in Patients With Coronary Artery Disease

Early Assessment and Treatment

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Acute heart failure syndromes (AHFS) have emerged as a leading public health problem worldwide, accounting for a substantial number of hospitalizations and a high utilization of resources. Although in-hospital mortality rates are relatively low, patients with AHFS have very high early after-discharge mortality and rehospitalization rates. The majority of patients admitted with AHFS have coronary artery disease (CAD), which independently has an adverse impact on prognosis. The initial in-hospital and after-discharge management of AHFS may be dependent on clinical presentation: AHFS in patients with underlying CAD or acute coronary syndromes (ACS) complicated by heart failure. In addition, the extent and severity of CAD and the presence of ischemia and/or stunned/hibernating myocardium should be assessed for optimal management. Although the overall management of AHFS with CAD may be similar to that in patients with ACS complicated by heart failure, for which specific guidelines exist, management of the former is less well defined. Prospective studies of the assessment and treatment of CAD in patients with AHFS are urgently needed. (J Am Coll Cardiol 2009;53:254–63) © 2009 by the American College of Cardiology Foundation

Acute heart failure syndromes (AHFS) can be defined as a rapid or gradual change in signs and symptoms in patients with chronic heart failure (HF) or new-onset HF that necessitates urgent therapy (1). Acute HF syndromes are a

leading and increasingly common cause of hospitalization worldwide. Despite considerable expenditures and intensive investigational efforts, hospitalization for AHFS continues to be associated with a poor prognosis (2–5). The mortality rate after hospitalization for AHFS has been reported to be

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as high as 15% and 35% at 30 days and 1 year, respectively, in patients already receiving pharmacologic therapy (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and beta-blockers) (4,5).

AHFS represent a heterogeneous group of patients in terms of their clinical presentation, pathophysiology, prognosis, and therapeutic options (1). The majority of patients presenting with AHFS have coronary artery disease (CAD). These patients may present in 1 of 2 ways: acute coronary syndromes (ACS) complicated by HF or AHFS with underlying CAD. The role of CAD in AHFS has not been well studied in clinical trials. Therapies that have shown to significantly improve morbidity and mortality, including pharmacologic and device therapies, have been studied in patients with chronic ambulatory HF with or without CAD. Given the severity of hemodynamic and neurohormonal activation in acute versus chronic HF, assessing for the presence, extent, and severity of CAD in patients with AHFS may have important therapeutic implications for the initial (emergency department), in-hospital, and after-discharge management.

The cornerstone of the evaluation of CAD in ACS is coronary angiography. The evaluation of CAD in AHFS with coronary angiography, often in conjunction with non-invasive functional imaging to detect ischemic or dysfunctional but viable myocardium, may represent an emerging approach to the assessment and management of AHFS patients. Current practice guidelines (6–11) have considerable overlap with respect to patients with HF. Although these guidelines provide recommendations on the use of coronary angiography for more appropriate use of pharmacological and/or myocardial revascularization in patients with chronic HF, they do not specifically address the timing and selection for these measures in patients with AHFS and CAD (6–11).

This document represents a consensus summary of discussions that occurred during the fourth International Acute Heart Failure Syndromes Working Group meeting in Chicago, Illinois, in April 2007.

AHFS

Epidemiology. AHFS account for more than 1 million hospitalizations per year in the U.S. and a similar number in Europe (12). They are the most common cardiovascular cause of hospitalization in the U.S., with a median stay of 3 to 4 days (1). AHFS is also the most common overall cause of hospitalization in adults 65 years and older, accounting for more than 5% to 10% of all admissions (13). Approximately 80% of patients hospitalized with AHFS carry a previous diagnosis of HF. In 15% of patients the diagnosis of HF is new, and the remaining 5% are admitted with advanced or refractory HF (1). The highest relative risk for mortality occurs within 30 to 60 days after discharge (1,2). The total direct and indirect health care costs of HF in the U.S. for 2006 have been estimated to be \$29.6 billion, with

the great majority of costs attributable to hospitalization (14). As the burden of AHFS increases with the aging population, the importance of evidence-based strategies to prevent HF exacerbations, decrease hospitalizations, contain costs, and improve outcomes has become an urgent public health issue.

Prognosis. The long-term prognosis for chronic HF patients with left ventricular (LV) systolic dysfunction has improved over the past 10 to 20 years, largely because of improved pharmacological therapy, advanced cardiovascular surgical and interventional techniques, and the use of implantable cardiac-defibrillators and cardiac resynchronization therapy (15,16). Despite these advances, hospitalization for HF is one of the most important predictors for rehospitalization and mortality (2–5). In several recent large registries (17–19), AHFS had a 4% to 7% in-hospital mortality rate. Survivors of hospitalization with AHFS have an early after-discharge mortality as high as 10% to 15% and rehospitalization rates of 30% at 60 to 90 days. One-year mortality rates in community cohorts and registries have ranged from 30% to 40% (4,5). Randomized controlled trials investigating the role of novel intravenous vasoactive compounds and the routine use of pulmonary artery catheters in the management of AHFS have failed to demonstrate improved survival or decreased length of hospitalization (20–25). In addition, serious concerns regarding the safety of intravenous vasoactive compounds in the setting of AHFS, especially in those patients with pre-existing CAD, have been raised (22,23,26). The traditional targets for therapy in AHFS are congestion and/or low cardiac output. Although interventions that improve hemodynamics are important for the alleviation of the signs and symptoms of HF, they may not prevent myocardial or renal injuries, which are often present in AHFS. As a consequence, these interventions may not only be ineffective in improving clinical outcomes but may even be deleterious (26–28).

Ventricular function. Although the majority of trials in AHFS conducted to date (19,29–35) studied patients with reduced systolic function, relatively preserved systolic function is present in approximately one-half of all patients hospitalized with AHFS. Approximately 60% of these patients have documented CAD (32). Over the past 20 years, the relative proportion of patients with AHFS and preserved systolic function has steadily risen relative to those with LV systolic dysfunction (29). This rise has corresponded with increased rates of CAD, hypertension, diabetes, and atrial fibrillation among patients with AHFS (36). Multiple registries have

Abbreviations and Acronyms

ACS	= acute coronary syndrome(s)
AHFS	= acute heart failure syndrome(s)
CABG	= coronary artery bypass graft
CAD	= coronary artery disease
CTA	= computed tomography angiography
HF	= heart failure
LV	= left ventricular
MI	= myocardial infarction
MRI	= magnetic resonance imaging

demonstrated that the risk of early death and long-term risk of death or rehospitalization in AHFS is similar for patients with preserved systolic function and LV systolic dysfunction (29,32–34). In the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry (30), the risk of in-hospital death in patients with AHFS and preserved systolic function was slightly lower than in those with AHFS and LV systolic dysfunction (2.9% vs. 3.9%). However, among survivors of the index hospitalization, the risk of death (~10%) and rehospitalization (~30%) in the first 60 to 90 days after hospital discharge was the same in the 2 groups (30). These patients, however, are more likely to die from other cardiac comorbidities, including CAD, rather than HF (37,38).

AHFS and CAD

Hospitalization. Coronary artery disease has emerged as the dominant etiologic factor in patients with HF. Pooling data from 24 multicenter trials of chronic HF over the past 20 years with >43,000 patients (1,36) revealed that 62% carried a diagnosis of CAD. This number is an underestimation of the prevalence of CAD in this population, as in clinical practice and in most studies there is no systemic assessment of coronary artery anatomy. Patients hospitalized with AHFS have a worse prognosis when they also carry a diagnosis of CAD (39). Long-term survival in patients with HF is directly related to the angiographic burden of CAD, although this observation may reflect only the extent of CAD in the epicardial vessels (40,41). Survivors of acute myocardial infarction (MI) not complicated by HF have a relatively high incidence of subsequent HF hospitalization, which is associated with significantly increased mortality (42).

In a study of 136 patients younger than 75 years of age hospitalized with incident HF, Fox et al. (43) combined clinical, angiographic, and myocardial perfusion imaging data to determine that CAD was the primary etiology in at least 52% of cases. Of note, in this study, 67% of patients who underwent angiography had anatomically significant CAD (defined as $\geq 50\%$ luminal stenosis), identifying CAD as a therapeutic target in AHFS even when it was not the primary etiologic factor. From the OPTIMIZE-HF registry of AHFS patients, in which less than one-half had known CAD, Fonarow et al. (44) identified ischemia as the primary precipitant for hospitalization in 15% of patients. These patients had significantly worse in-hospital and 60- to 90-day after-discharge mortality. Although these data indicate that CAD may cause or precipitate AHFS, the contribution of CAD to clinical decompensation can be difficult to determine when multiple comorbid conditions are present.

After-discharge events. There is no single explanation for the high mortality and rehospitalization rates in patients who survive hospitalization for AHFS. It is possible that CAD is an important contributor to this high after-discharge event rate. An autopsy study of 180 patients with

Table 1	Characteristics of Patients With AHFS and CAD Versus Patients With ACS Complicated by HF	
	AHFS and CAD	ACS Complicated by HF
Dyspnea	Common	Common
Chest discomfort	Uncommon	Common
Prior HF	Common	Uncommon
BNP/N-terminal proBNP	Elevated	Elevated
Troponin	Normal or elevated*	Usually elevated
Left ventricular systolic function	Normal or depressed	Normal or depressed
Diagnostic testing for CAD† (ischemia/viability/angiography)	Uncommon	Standard (per guidelines)
Myocardial revascularization	Uncommon†	Standard (per guidelines)
Secondary prevention for CAD	Underused	Standard (per guidelines)
In-hospital mortality	Relatively low	Relatively high
Early after-discharge death or rehospitalization	High	High

*Typically low-level elevation. †During index hospitalization.

ACS = acute coronary syndrome; AHFS = acute heart failure syndrome; BNP = B-type natriuretic peptide; CAD = coronary artery disease; HF = heart failure.

known ischemic cardiomyopathy (45) revealed that acute MI was responsible for 57% of the deaths. This study revealed that many deaths due to acute MI in patients with HF were misclassified as due to progressive HF or arrhythmias. In the ATLAS (Assessment of Treatment with Lisinopril and Survival) study (46), 54% of patients with chronic HF and CAD who died suddenly had autopsy evidence of acute MI.

In a group of patients with HF and LV systolic dysfunction, 25% of repeat hospitalizations were attributed to ACS (47). Approximately 10% of patients subsequently hospitalized for ACS were originally classified as nonischemic. The in-hospital mortality rate in this group was 36%. These data suggest that patients with AHFS can be mislabeled as nonischemic or that CAD may either develop or progress in patients with nonischemic cardiomyopathies (48).

Pathophysiology: AHFS and CAD

The majority of patients with AHFS and CAD are not hospitalized or diagnosed with ACS. There are, however, considerable similarities between non-ACS AHFS patients and ACS patients complicated by HF (Table 1). In contrast with ACS complicated by HF, where myocardial injury is the principal cause for HF, the myocardial injury in AHFS in patients with underlying CAD may be related to worsening HF. The injury may be the result of marked hemodynamic and neurohormonal abnormalities known to occur in the setting of AHFS but less likely to be present in chronic HF. In AHFS, the high LV diastolic pressure often results in subendocardial ischemia, which is associated with further activation of neurohormones. This activation can increase cardiac contractility and reduce coronary perfusion through endothelial dysfunction. In addition, patients with AHFS and CAD often have hibernating or stunned myo-

cardium (28). Together, all of these factors may result in myocardial injury (1).

Hypotension in AHFS patients is associated with increased mortality (49). Coronary perfusion may be further impaired in AHFS in the setting of low systemic blood pressure. In this setting, the autoregulation between coronary artery perfusion pressure and coronary vasoactive tone may be lost or impaired in patients with obstructive epicardial CAD (28). This may explain why patients with AHFS and CAD frequently have troponin elevation. These troponin elevations most likely represent myocardial injury and are associated with worse outcomes (50–55). In the PRESERVED-HF (Pilot Randomized Study of Nesiritide Versus Dobutamine in Heart Failure) trial, 74% of non-ACS patients with AHFS and known CAD had low-level troponin elevation at the time of hospital admission (54). Of the 26% who did not initially have troponin elevation, 42% had troponin elevation within 72 h (for a total of 85% of all patients within 72 h of admission). Data from ADHERE (Acute Decompensated Heart Failure National Registry) (55) indicate that patients admitted with AHFS not thought to have ACS but with troponin elevations that exceed the laboratory threshold for acute MI have significantly higher in-hospital mortality (8.0% vs. 2.7%, $p < 0.001$).

It appears that a history of myocardial revascularization in patients with AHFS is associated with improved outcomes (53,56). The lack of typical angina despite myocardial injury in AHFS patients may be due to the predominance of respiratory symptoms; the high incidence of diabetes; and the use of medications, including nitrates and beta-blockers, that may blunt angina. When it does occur, chest pain in AHFS patients is often a sign of myocardial injury. In one study (57), 32% of patients with chronic HF presenting to the emergency department with chest pain were diagnosed with ACS.

Pathophysiology: ACS Complicated by HF

Approximately 10% to 20% of patients with ACS have concomitant HF, and up to 10% of ACS patients develop HF during hospitalization (58–63). In the EuroHeart Survey II on HF (64), 37% of patients had de novo HF, 42% of which was attributable to ACS. Patients with ACS and ST-segment elevation typically have high levels of cardiac biomarker elevation, corresponding to high levels of myocardial injury. Of ACS patients with HF but without ST-segment elevation, more than two-thirds have significant cardiac enzyme elevation (troponin >3 times the upper limit of normal), a proportion similar to those presenting without HF (52). The majority of these patients do not have a history of HF and have preserved systolic function (58,60). The short-term risk of adverse clinical outcomes in patients with ACS complicated by HF is directly proportional to the level of troponin elevation (65).

Patients with ACS complicated by HF have markedly increased short- and long-term mortality rates compared with those without HF (58–60,66–73). Patients who de-

velop HF after presentation have even higher mortality than those presenting with ACS and HF (59,63). The prognosis of ACS complicated by HF is directly related to the degree of HF as measured by the Killip classification (59,61,63). Compared with those with Killip class I HF, patients with an ACS in Killip class II or III HF are 4 times more likely to die during the index hospitalization, whereas those with cardiogenic shock (class IV) have a 10-fold higher mortality (60,63). Furthermore, among ACS patients who recover from transient HF, the majority develop recurrent HF (42).

Assessment of CAD in AHFS

Currently, there are no consensus statements or practice guidelines on the most appropriate timing and methods to detect or reassess CAD in patients with AHFS. Most studies have used clinical criteria, including a history of MI, angina, or myocardial revascularization, or the results of exercise testing and/or noninvasive imaging to determine which patients with AHFS have CAD. This approach may contribute to the underdiagnosis of CAD and its severity in this population.

Electrocardiography and echocardiography are the most common cardiac diagnostic tests obtained in patients with AHFS (19). Patients with LV systolic dysfunction and electrocardiographic Q waves usually have significant CAD (74). However, most patients with HF and CAD do not have Q waves, whereas those with nonischemic cardiomyopathies can have Q waves (74). Similarly, segmental wall motions identified by echocardiography are predictive of CAD, but not its extent and severity (74,75).

Coronary Angiography

Coronary angiography is the gold standard for the diagnosis and reassessment of CAD against which all other modalities are compared (41). In patients with HF, the long-term prognosis is directly related to the angiographic extent and severity of CAD (40,41). This has been demonstrated in HF patients with LV systolic dysfunction and preserved systolic function (76). A clinical strategy in the evaluation of AHFS that does not assess for the presence, extent, and severity of CAD may grossly underestimate its prevalence. Despite the existing guidelines and the high incidence of CAD in patients with AHFS, angiography is used infrequently for the assessment or reassessment of CAD (6). In 3 large AHFS registries, coronary angiography was performed in only 9% to 16% of patients during the index hospitalization (1,19). Similarly low rates of angiography have been observed in a community-practice setting for patients with newly diagnosed AHFS (77). Patients with ACS complicated by HF are less likely to undergo coronary angiography and revascularization and to receive pharmacological therapy for CAD than ACS patients without HF (62,63,73,78,79). In the OPTIMIZE-HF registry, it has been preliminarily reported (80) that performance of coro-

nary angiography during the index hospitalization for AHFS was associated with an increased utilization of aspirin, statins, and myocardial revascularization and a reduced risk of death at 60 to 90 days after discharge. This raises the hypothesis that the knowledge of the extent and severity of CAD in AHFS patients will have an important role in treatment decisions.

Multidetector coronary computed tomography angiography (CTA) has been shown to be highly accurate to determine the presence or absence of CAD in patients with HF (81). However, when CAD is present, the ability of CTA to define its extent and severity is hampered by unseen segments and artifacts caused by motion and calcium (82). This role of coronary CTA in this population may be an important focus of future investigations, but currently cannot be recommended in lieu of coronary angiography at this time.

Myocardial Ischemia

In patients with AHFS and evidence of ischemia, the diagnosis of obstructive CAD by angiography should lead to the consideration of early myocardial revascularization and aggressive medical therapy with antiplatelet agents and statins in addition to beta-blockers and ACE inhibitors/angiotensin receptor blockers. In the absence of clinical signs of ischemia, additional testing may be needed to guide therapeutic choices (83). Dobutamine stress echocardiography detects ischemia through the induction of new or exaggerated LV wall motion abnormalities during stepwise infusion of dobutamine. Nuclear perfusion imaging with single-photon emission computed tomography uses intravenously delivered radioisotopes (thallium-201 chloride or technetium-99m labeled tracers); regions with defects following stress that normalize at rest are indicative of ischemia. More recently, positron emission tomography has also been used to assess ischemia, employing tracers such as rubidium-82, N13-ammonia, or O15-labeled water. Vasodilator stress magnetic resonance imaging (MRI) is a newer noninvasive stress imaging modality that has not yet been studied in HF patients for the assessment of ischemia (84).

Myocardial Viability

The presence of viable but dysfunctional myocardium can be used to predict a favorable response to myocardial revascularization and pharmacological therapy (85–87). Left ventricular systolic dysfunction can be secondary to repetitive stunning or hibernation. In this setting, stunning is defined as reversible LV dysfunction attributable to repetitive episodes of ischemia, whereas hibernating myocardium is defined as reversible LV dysfunction caused by chronic hypoperfusion (88). Up to 50% of patients with CAD and chronic LV dysfunction have significant areas of dysfunctional but viable myocardium (89). Hibernating myocardium is associated with global alterations in LV volumes and shape, not just impairment of underperfused ventricular segments (88). This explains why myocardial revasculariza-

tion of hibernating territories can promote reverse remodeling globally (90).

The identification of viable myocardium is based on detection of its characteristics, which include intact perfusion, cell membrane integrity, intact mitochondria, preserved glucose metabolism and contractile reserve (85,88,91,92). Intact perfusion, cell membrane integrity, and intact mitochondria can be evaluated with single-photon emission computed tomography imaging using thallium-201 chloride and/or technetium-99m labeled tracers. Preserved glucose metabolism can be assessed by positron emission tomography using F18-fluorodeoxyglucose. Contractile reserve can be unmasked by infusion of low-dose dobutamine during echocardiography. The use of these techniques has been associated with improved survival in patients with chronic HF and significant viability who underwent myocardial revascularization (85,88,91,92).

Cardiac MRI is another technique to assess myocardial viability (93,94). Resting cine MRI can be used to assess LV end-diastolic wall thickness. It has been shown that an end-diastolic wall thickness <5 to 6 mm is a marker of transmural MI and virtually excludes the presence of viable myocardium. In dysfunctional myocardium with preserved end-diastolic wall thickness (≥6 mm), detection of contractile reserve during low-dose dobutamine infusion confirms the presence of viable myocardium. Gadolinium-based contrast agents have been used to detect nonviable myocardium, as these agents accumulate selectively in areas of scar tissue. It should be noted that this technique is extremely sensitive to detect scar tissue (with very high spatial resolution), but the absence of scar tissue does not permit discrimination between normal tissue and hibernating or stunned myocardium (93).

Treatment of CAD in AHFS

Pharmacologic therapy. The presence of CAD in patients with AHFS may have a profound impact on treatment. Considering the overlap in pathophysiology, including increased platelet reactivity, myocardial ischemia and injury,

Table 2	Therapies for AHFS and CAD Versus ACS Complicated by HF	
	AHFS and CAD	ACS Complicated by HF
Immediate therapies		
Nitrates	Yes	Yes
Antiplatelet agents	Yes	Yes
Anticoagulation	No	Yes
Inotropes	Avoid if possible	Avoid if possible
Statins	Yes	Yes
Renin-angiotensin system modulation		
ACE-I or ARB	Yes	Yes
Aldosterone blockade (if LVSD)	Yes	Yes
Beta-blockers	Yes	Yes
Early angiography/revascularization	Yes*	Yes*

*If jeopardized myocardium present (ischemia or viability).
ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; LVSD = left ventricular systolic dysfunction; other abbreviations as in Table 1.

impaired coronary perfusion, and elevated LV filling pressure, the treatment approach for AHFS with CAD can be modeled after the standard approach for ACS (Tables 1 and 2). This may include the early administration of antiplatelet therapy in AHFS patients with known CAD or suspected ischemia (95).

The immediate management of AHFS usually occurs in the emergency department. In patients with underlying CAD who are not hypotensive, nitrates may be the ideal initial agents. Nitrates provide rapid reduction of myocardial ischemia and can improve coronary perfusion. In patients with severe pulmonary edema, the combination of high-dose nitrates and low-dose diuretics (vs. low-dose nitrates and high-dose diuretics) led to a decreased need for mechanical ventilation and significantly lower rates of MI (96). A regimen consisting of lower doses of diuretics has been proposed as a method of preserving renal function in AHFS. In a large AHFS registry, the use of intravenous nitroglycerin or nesiritide was associated with lower in-hospital mortality compared with treatment with dobutamine or milrinone (97). However, compared to intravenous nesiritide in AHFS patients (>60% with documented CAD), intravenous nitroglycerin has been associated with less deterioration of renal function and a trend toward less mortality at 30 days (23,98,99).

Inotropes may be particularly harmful when used in patients with AHFS and CAD. Experimentally, the use of dobutamine in a model of HF with hibernating myocardium led to increased myocardial necrosis (27). Patients with AHFS and troponin elevation have significantly higher in-hospital mortality when inotropes are used (55). In the OPTIME-CHF (Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure) trial (26), the phosphodiesterase inhibitor milrinone was assessed during AHFS. In patients with CAD, milrinone was associated with increased after-discharge mortality compared with placebo. In general, a decrease in coronary perfusion as a result of a decrease in blood pressure and/or an increase in heart rate, often resulting from inotropes with vasodilator properties or inotropes used in conjunction with vasodilators, may be particularly deleterious in patients with AHFS and CAD (26,100).

The pre-discharge initiation of optimal medical therapy for HF, including beta-blockers and ACE inhibitors or angiotensin receptor blockers, is associated with improved medication adherence and an early survival advantage (80,101–103). The continuation of beta-blocker therapy in patients hospitalized with AHFS is associated with lower after-discharge mortality risk (104). Also, the addition of the aldosterone blocker eplerenone to optimal medical therapy in ACS patients complicated by HF and LV systolic dysfunction was shown (105) to significantly reduce overall mortality, sudden cardiac death, and rehospitalization.

Medical regimens for CAD can differ according to HF status. Acute coronary syndrome patients complicated by HF are less likely to receive antiplatelet agents, beta-blockers, ACE inhibitors, or statins than are ACS patients

without HF (42,58,60,62,63). In the OPTIMIZE-HF registry (106), only 14,904 of 38,066 (39.2%) AHFS patients with documented CAD, hyperlipidemia, diabetes, or other atherosclerotic vascular disease were treated with statins.

Myocardial revascularization. The American College of Cardiology/American Heart Association and European Society of Cardiology practice guidelines for coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention do not specifically address patients with CAD and AHFS (9–11). Revascularization may improve outcomes in patient with HF and dysfunctional but viable myocardium. In a meta-analysis of >3,000 patients with LV systolic dysfunction, revascularization was associated with markedly decreased yearly mortality (3.2% vs. 16.0%, $p < 0.0001$) if viability was present (85). In patients without hibernating myocardium, revascularization did not improve survival. Recently, a retrospective observational study (107) examined the role of myocardial revascularization in ~4,000 patients with chronic HF. At 1 year, patients who underwent revascularization had substantially reduced mortality (11.8% vs. 21.6%, hazard ratio: 0.52, 95% confidence interval: 0.47 to 0.58). The survival curves continued to diverge through 7 years of follow-up. This data is limited by its retrospective nature. However, the ongoing prospective randomized STICH (Surgical Treatment for Ischemic Heart Failure) trial may help elucidate the role of revascularization in chronic heart failure patients with CAD and LV systolic dysfunction (36).

Revascularization is rarely performed during hospitalization for AHFS. In 3 large AHFS registries that included approximately 170,000 patients, only 2% to 4% of patients underwent coronary artery bypass graft surgery or percutaneous coronary intervention (1,14,108). Outcomes in patients with AHFS in the setting of ACS are improved by a strategy of early revascularization (109). Patients hospitalized with AHFS have improved early survival if they have a history of myocardial revascularization, although this is a retrospective finding (53,56). These data generate the hypothesis that early revascularization will be beneficial in AHFS patients with ischemia due to CAD. This hypothesis remains to be tested in a prospective randomized study of early myocardial revascularization in non-ACS patients with AHFS and CAD.

A strategy of early angiography and revascularization, where appropriate, in AHFS must take into account the potential risks and costs. The risk of vascular complications and contrast-induced nephropathy has steadily declined in recent years owing to technical and preventative advancements (110,111). The cost-effectiveness of such a strategy will probably depend most on its impact, if any, on rehospitalization rates. The use of coronary angiography during hospitalization for AHFS is associated with a decreased risk of early rehospitalization (80), but this also needs to be prospectively studied. A formal strategy to detect or reassess the extent and severity of CAD in patients

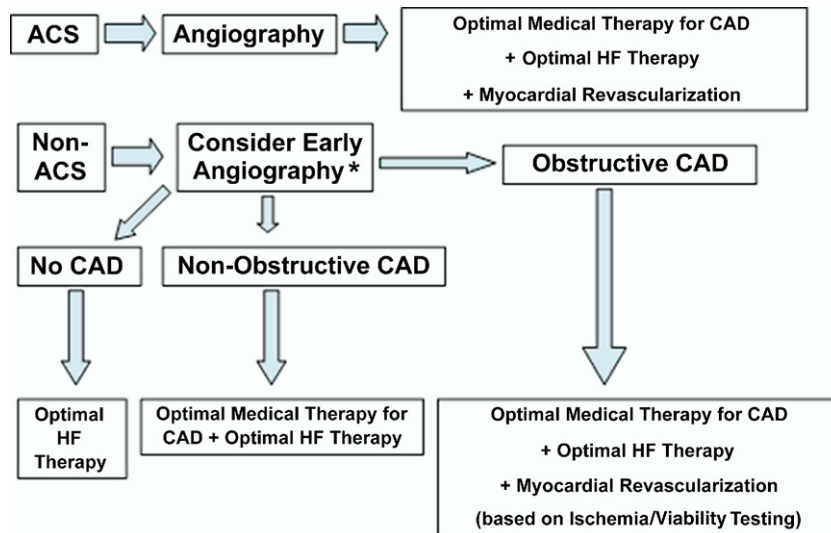


Figure 1 Therapeutic Strategies in Patients With AHFS

*For those patients with remote or no history of coronary angiography. ACS = acute coronary syndrome; CAD = coronary artery disease; HF = heart failure.

with AHFS may improve the implementation of evidence-based therapies that can improve clinical outcomes (Fig. 1).

Conclusions

AHFS have emerged as a leading public health problem worldwide, accounting for a substantial number of hospitalizations and a high utilization of resources. A significant number of patients admitted with AHFS have CAD and can be divided into those who present with or without ACS. Both groups have high early after-discharge mortality and rehospitalization rates. Knowledge of the extent and severity of CAD and the presence of ischemic and/or stunned/hibernating myocardium may influence the initial and in-hospital management of these patients. Although specific guidelines exist for patients with ACS complicated by HF, prospective studies of the assessment and treatment of CAD in the setting of acute HF are urgently needed.

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